Author's response to reviews

Title: Novel TBX1 loss-of-function mutation causes isolated conotruncal heart defects in Chinese patients without 22q11.2 deletion

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Author's response to reviews: see over
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Editor of
BMC Medical Genetics

Dear Editor,

We appreciated all the enlightening comments from the editors. The manuscript has been revised according to the comments. The modified parts were highlighted in blue. We also responded point by point to each reviewer comments as listed below. Thank you very much.

Best regards

Yours sincerely,

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Response to reviewer's comments:

Reviewer: Maria Cristina Digilio
Comments to the Author
1. The report is noteworthy as short observation, but more clinical details regarding the mutated subject should be added.

Author's response:
We have added the clinical details in the revised manuscript. Please see the first paragraph of the “Results” section.

2. Clinical criteria of inclusion of patients are weak (the authors state that patients had CHD without deletion 22q11.2 and no extracardiac anomalies were present. ) Which kind of extracardiac anomalies were absent?

Author’s response:
We have made changes in the revised manuscript. Please see the “Subjects” of the “Methods” section.

3. Can the authors provide clinical details of facial appearance of the mutated patients? I realize that it is probably difficult to obtain, but a photo of the face of this patient should be useful.

Author’s response:
The patient’s face looked normal. Please see the first paragraph of the “Results” section.
This family came from Luoyang city, Henan province. The patient was a 12 years old boy and died in the second year after discharge. He had no brother or sister. His parents refused to put his photo in the manuscript. So we did not add the photo.

4. How was excluded mild cognitive of deficit?

Author’s response:
We have made changes in the revised manuscript. Please see the first paragraph of the “Results” section. The patient’s height and weight was normal (Height 152cm, Weight 50kg). He didn’t show mental retardation. But he did not finish his primary school due to the cardiac defects. We couldn’t do intelligence test for him, because he was diead at 13 years old.
Thank you very much.

Reviewer: Edward Lammer

Comments to the Author
1. The introduction and discussion should include comments and references to CRKL, another gene that is within the common 3MB 22q11 microdeletion and that has been associated with conotruncal defects when deleted, even if TBX1 is not affected.

Author’s response:
We have sequenced the coding regions of the human CRKL gene. However, we didn’t find any mutation of the CRKL.
We have made changes accordingly in the manuscript. Please see the “Background” and of the “Abstract” section, the third paragraph of the “Background” section, the “Sequencing” part of the “Methods” section, the third paragraph of the “Results” section, and the last two paragraphs of the “Discussion” section.
The primers used to amplify the coding region of the CRKL gene were listed in the Table 1.
In the “Reference” section, we have added the 7 references about CRKL (Reference 7-11, and 34, 35). Thank you very much.